Page 7 of 25

REMARKS

Claims 1, 14, and 15 have been canceled. Claim 1 has been canceled as being drawn to a nonelected invention. Applicants expressly reserve the right to file a divisional application directed towards the subject matter of this claim. Claims 14 and 15 have been canceled without prejudice to or disclaimer of the subject matter contained therein in order to expedite prosecution. Claims 2-7, 11-13, and 20-22 have been amended. Claims 23-26 have been added. Support for the recitation of high stringency hybridization conditions and the recitation of increased seed yield may be found in the specification, for example on page 12, lines 3-5, and page 3, lines 20-30, respectively. Support for the recitation of fragments of at least 50 contiguous nucleotides of SEQ ID NO:1 may be found in the specification on page 7, line 12. Support for new claims 23-26 may be found in original claims 11, and 20-22 respectively. No new matter has been added by way of amendment or presentation of new claims.

Claims 2-13 and 16-26 are now pending in the application. Reexamination and reconsideration of these claims are respectfully requested. The Examiner's remarks in the Office Action are addressed below in the order set forth therein.

The Rejections of the Claims Under 35 U.S.C. §112, First Paragraph, Should Be Withdrawn

Claims 2-22 have been rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description. Specifically, the Examiner states that, although Applicants have provided adequate written description for SEQ ID NO:1, adequate written description has not been provided for the following four categories of sequences: 1) nucleotide sequences with at least 80% sequence identity to SEQ ID NO:1; 2) nucleotide sequences corresponding to an antisense sequence of SEQ ID NO:1; 3) nucleotide sequences encoding a yeast invertase; and, 4) nucleotide sequences that hybridize under unspecified stringency conditions to any of the sequences of categories 1) - 3), or complementary sequences thereof. This rejection is respectfully traversed as applied to the amended claims.

At the outset, Applicants note that adequate written description of a claimed genus of nucleotide sequences can be made via structure, formula, chemical name, or physical properties.

Page 8 of 25

See Ex parte Maizel, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), citing Amgen v. Chugai, 927 F.2d 1200, 1206 (Fed. Cir. 1991). Thus, as the Examiner has noted in the present Office Action, a genus of DNAs may be described by means of a recitation of a representative number of DNAs, defined by nucleotide sequence, falling within the scope of the genus, or by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. See Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997); see also Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2000).

The written description requirement of 35 U.S.C. §112, first paragraph, may also be satisfied by a recitation of functional characteristics in the description, provided there is a correlation between the function and structure of the claimed invention. *Id.*, *citing Lilly* at 1568. Example 14 of the *Revised Interim Written Description Guidelines* (available at www.uspto.gov/web/menu/written.pdf, page 53), for example, is directed to a generic claim of a protein having high sequence identity to the sequence of SEQ ID NO:3, *wherein the sequence catalyzes the reaction A→B*. The *Guidelines* concludes that the generic claim of Example 14 is sufficiently described under §112, first paragraph, because 1) "the single sequence disclosed in SEQ ID NO:3 is representative of the genus," and 2) the claim recites a limitation requiring the compound to catalyze the reaction from A→B. Thus, on the basis of the limitations provided in Example 14, one of skill in art would recognize that the patentee was in possession of the necessary common attributes possessed by the members of the genus, in satisfaction of the written description requirement.

With regard to the four categories of sequences recited by the Examiner, the sequences in each of these categories have been disclosed in sufficient structural detail to support a finding of adequate written description. Thus the nucleotide sequences of category 1 are specifically disclosed as a genus of structures derived from the sequence of SEQ ID NO:1 and structurally related to this sequence by a percent identity of 80% or higher. Furthermore, Applicants have now amended the claims to recite that these sequences having 80% or higher sequence identity to SEQ ID NO:1 additionally encode a polypeptide having invertase inhibitor activity, a functional

Page 9 of 25

limitation that falls within the second category above for adequate written description. With regard to the antisense nucleotide sequences of category 2 and the hybridizing sequences of category 4, these sequences are constrained by the specific structural requirement of hybridization under conditions of high stringency with the corresponding mRNA for the antisense sequences of category 2 (see specification, page 5, lines 34-35), or with the DNA for SEQ ID NO:1 or a complement thereof. Finally, with regard to the recitation of yeast invertase sequences of category 3, now presented in new claims 23-26, the structure of these sequences is provided in structural detail in the Weber *et al.*, Sonnewald *et al.*, von Schaewen *et al.*, Silveira *et al.*, Roitsch *et al.*, and Tussig *et al.* references recited in the specification on page 4, lines 14-17. These structures provide a sufficient disclosure of written description to satisfy the requirements of 35 U.S.C. §112, first paragraph, for the nucleotide sequences of categories 1) -4).

Applications note that arguments similar to those presented above also apply to any written description rejection that may be raised with regard to the fragments of at least 50 contiguous nucleotides of SEQ ID NO:1 that are now recited in claims 2, 11, and 20-22 as amended. Specifically, such fragments are all based on the recited structure of SEQ ID NO:1, and therefore are presented in sufficient structural detail to meet the requirements of 35 U.S.C. §112, first paragraph, written description.

In light of this discussion regarding the specific presentation of structural and functional description for each of these four categories of sequence recited by the Examiner, as well as for the fragments of SEQ ID NO:1 also discussed above, it is clear that all of the sequences recited in the claims find adequate written description in the specification. Thus the rejection under 35 U.S.C. §112, first paragraph, written description, should be withdrawn.

Claims 2-22 have been rejected under 35 U.S.C. §112, first paragraph, as lacking adequate enablement. Specifically, the Examiner has asserted that undue experimentation would be required: 1) to isolate a multitude of non-exemplified invertase inhibitor sequences with at least 80% sequence identity to SEQ ID NO:1 and to evaluate their ability to encode a protein

Page 10 of 25

with invertase inhibitor activity, or a multitude of sequences which hybridize under low or moderate stringency conditions thereto (Office Action of October 23, 2002, last three lines on page 6, continuing through first line on page 7); and, 2) to evaluate a multitude of non-exemplified regenerated plants with modulated invertase activity and/or increased yield (Office Action of October 23, 2002, page 6). These rejections are respectfully traversed as applied to the amended claims.

Applicants note at the outset that the standard for experimentation as it relates to the enablement requirement of 35 U.S.C. §112, first paragraph, is not whether experimentation occurs at all, but rather whether such experimentation, even when extensive, is undue. Thus, although some techniques might in some situations be labor intensive, the Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for experimentation, as long as the experimentation needed to practice the invention is not undue. In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed Cir. 1988). Consequently, a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. Id.

With regard to the amount of experimentation required to isolate and characterize non-exemplified invertase inhibitor sequences encoding a protein with invertase inhibitor activity, Applicants submit that, in light of the *routine* nature of the methods disclosed in the specification and known to one of ordinary skill in the art for obtaining such molecules, the amount of experimentation required for their isolation and characterization is not undue, and these portions of the claims are therefore enabled.

Thus, the specification discloses SEQ ID NO:1 and a variety of ways of generating sequences having at least 80% sequence identity to this invertase inhibitor, as well as assays for routinely determining the functionality of such molecules. See, e.g., the specification, page 9, line 13-14. Furthermore, one of ordinary skill in the art would be well acquainted with such methods, and would find their practice to be routine. For example, the skilled artisan would know a variety of standard techniques for generating % sequence identity variants of the invertase inhibitor molecule of the invention, and would also know that there are numerous

Page 11 of 25

techniques available for the routine screening of such molecules for invertase inhibitor activity. Furthermore, having disclosed SEQ ID NO:1, one of skill in the art could readily isolate sequences that hybridize to this sequence, or a complement thereof, under the specified stringent conditions recited in the claims, using procedures well known in the art and further disclosed in the specification. See, e.g., the specification at pages 10-13. Applicants note that similar arguments also apply to any enablement rejection that may be raised with regard to the fragments of at least 50 contiguous nucleotides of SEQ ID NO:1 that are now recited in claims 2, 11, and 20-22 as amended.

In view of the disclosure of the specification and the knowledge of those skilled in the art, sufficient guidance would be available to the skilled artisan to identify other invertase inhibitor coding sequences and the recited hybridizing sequences in a *routine* manner. Given the enabling nature of such routine experimentation, this portion of the rejection should be withdrawn.

With regard to the enablement of the claims directed to "a multitude of non-exemplified regenerated plants with modulated invertase activity and/or increased yield" (original claims 20-21 and new claims 24-25), Applicants note at the outset that the references cited by the Examiner as evidence of the unpredictability of obtaining invertase modulation or increased yield in fact do not teach such unpredictability, and therefore should not be used as the basis of a finding of nonenablement for these claims. Specifically, although Sander *et al.* ((1996) *FEBS Letts*. 385:171-175) demonstrate that two different invertase inhibitors have different *mechanisms* for inhibiting invertase activity, it is not clear how this result would render unpredictable the ability to modulate invertase activity or increase yield by, for example, inhibiting the expression of one or more invertase inhibitors. In this regard, Applicants note that Sander *et al.* (page 171, first paragraph) state that there is a common evolutionary origin for different invertase inhibitor types. This finding would tend to support the uniformity of invertase inhibitor molecules, suggesting that at least one method contemplated for modulating invertase expression or increasing yield – the inhibition of invertase inhibitor activity – might be expected to act broadly on more than one invertase inhibitor molecule.

Page 12 of 25

Similarly, although von Schaewen et al. ((1990) EMBO J. 9:3033-3044) and Weber et al. ((1998) Plant J. 16:163-172) do teach a variety of effects of the expression of a yeast invertase gene in dicots, these results do not render unpredictable the modulation of invertase activity and increased seed yield in accordance with the methods of the present invention. For example, although von Schaewen et al. does describe tobacco plants with stunted growth and bleached and/or necrotic regions in older leaves, which the Examiner has apparently taken as an indication of yield reduction, in fact there is no indication as to the effects on seed yield. Weber et al. describes the results of experiments in another dicot, Vicia narbonensis, which the Examiner states show "a negative impact upon yield with respect to the storage of both proteins and starch." Office Action, page 6. However, while it is true that Weber et al. does state that "[d]espite the higher activity of sucrose mobilisation there was a strong negative effect on storage activity, predominantly starch but also on storage protein accumulation," Weber et al. page 169, first column, second section, this same reference demonstrates that other cotyledon components are present in substantially increased yield in these experiments, e.g., glucose levels are increased 100-fold, fructose 5-10-fold, glucose 6-phosphate and fructose 6-phosphate 3-7fold. Id. at page 165, second column, first full paragraph. Thus the fact that Weber et al. shows that "invertase expression severely *changed* the carbohydrate state of the cotyledons by increasing the hexose to sucrose ratio and decreasing starch" (emphasis added) cannot be said to teach the unpredictability of modulating invertase activity or increasing seed yield in the manner set forth in Applicants' claimed invention, as this conclusion merely shows a redistribution in carbohydrate partitioning.

Although the above discussion is sufficient to demonstrate that the claimed methods of modulation and increasing seed yield are adequately enabled, Applicants note that a second basis for the enablement of these claims may be found in the routine methods provided in the specification for accomplishing these goals. For example, the specification discusses the use of a variety of means for inactivating invertase inhibitors, thereby producing the positive modulation of invertase activity and yield, including antisense suppression (see the specification at pages 5-6) and co-suppression using an invertase inhibitor sequence in the sense orientation (see the

Page 13 of 25

specification at page 6), both of which are recited in the claims. Therefore, in light of these methods and the fact that, as discussed above, experimentation that is extensive but *routine* satisfies the enablement requirement of 35 U.S.C. §112, first paragraph, the enablement rejection as it applies to the claims directed to "a multitude of non-exemplified regenerated plants with modulated invertase activity and/or increased yield" (original claims 20-21 and new claims 24-25) should be withdrawn.

In summary, in light of the recitation of routine methods for accomplishing the goals of modulating invertase activity or increasing seed yield, and the statements presented above with regard to the references cited in the Office Action, it is clear that the claims are adequately enabled, and the rejection should be withdrawn.

The Rejections of the Claims Under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

Claims 2, 11, and 20-22 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite for failing to clearly define the meaning of the term "antisense sequence" in terms of its match to the sense sequence and its length, and for the use of the phrase "an antisense sequence" rather than "the antisense sequence."

With regard to the definition of the term "antisense sequence," Applicants submit that the specification clearly recites this term as being a nucleotide sequence "constructed to hybridize with the corresponding mRNA," with this functional limitation of hybridization emphasized by the fact that "[m]odifications of the antisense sequences may be made as long as the sequences hybridize to and interfere with expression of the corresponding mRNA." Specification, page 5, lines 34-37. Applicants also note that claims 2, 11, and 20-22 have been amended to recite a nucleotide sequence that is an antisense sequence, where the antisense sequence is specified as hybridizing to SEQ ID NO:1 under high stringency hybridization conditions in order to emphasize this hybridization requirement. Therefore, in light of the recitation of the meaning of the term "antisense sequence" in the specification, and the amendments to claims 2, 11, and 20-22 to recite hybridization under high stringency conditions, this portion of the rejection has been obviated, and should be withdrawn.

Page 14 of 25

With regard to the rejection for the use of the phrase "an antisense sequence," Applicants respectfully note that this portion of the claims encompasses more than one antisense sequence. Further, the amendment to these claims clarifies this point. As such, Applicants submit that this portion of the claim is definite, and that this rejection of the claims should be withdrawn.

Claims 11 and 14 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite for reciting "an antisense sequence for a plant invertase inhibitor," rather than "an antisense sequence of a sequence that encodes a plant invertase inhibitor." The portion of claim 11 containing this phrase has been removed by amendment, and claim 14 has been canceled. Thus this rejection has been obviated, and should be withdrawn.

Claim 15 has been rejected under 35 U.S.C. §112, second paragraph, as indefinite for reciting "the nucleotide sequence is a yeast invertase." In light of the cancellation of claim 15, this rejection has been obviated, and should be withdrawn.

Claims 3, 5, and 12 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite for reciting the limitation that the nucleotide sequence disclosed therein "encodes an invertase inhibitor." Applicants have removed this reference to an invertase inhibitor, so that the claim now recites that the nucleotide sequence encodes the amino acid sequence set forth in SEQ ID NO:2. On this basis the rejection has been obviated, and should be withdrawn.

Claim 4 has been rejected under 35 U.S.C. §112, second paragraph, as indefinite for the confusing use of the term "a sequence in a plant cell operably linked to a nucleic acid sequence of claim 2," and for the use of "a nucleotide sequence of claim 2." In keeping with the Examiner's suggestions, Applicants have amended claim 4 to contain the term "plant-functional" before promoter, have deleted the phrase "capable of driving expression of a sequence in a plant cell," and have changed the term "a nucleotide sequence of claim 2" to "the nucleotide sequence

Page 15 of 25

of claim 2." In view of these amendments, this rejection has been obviated, and should be withdrawn.

The Rejections of the Claims Under 35 U.S.C. §102 Should Be Withdrawn

Claims 2, 4, 8-11, 15-16, 19, and 20-22 have been rejected under 35 U.S.C. §102(b) as anticipated by Bussis *et al.* (1997) *Planta* 202:126-136. Specifically, the Examiner has indicated that, in light of the unspecified hybridization conditions recited in original claims 2(d), 11(g), 20(g), 21(g), and 22(g), these claims would encompass the yeast invertase sequence and dicot plant (potato) expressing this sequence disclosed in Bussis *et al.* Applicants have now amended these portions of the claims (now presented as claims 2(d), 11(e), 20(e), 21(e), and 22(e)) to recite high stringency hybridization conditions, thereby obviating this rejection, which should be withdrawn.

Claims 2, 4, 8-11, 14, and 16-22 have been rejected under 35 U.S.C. §102(a) as anticipated by Rausch *et al.*, WO 00/09719. In this regard, Applicants respectfully note that WO 00/09719 has a publication date of February 24, 2000, which *post-dates* Applicants' earliest effective filing date of February 10, 2000. Thus, this published international application cannot serve as the basis of a rejection under 35 U.S.C. §102(b), and the rejection should be withdrawn.

Claims 2, 4, 8-11, 14, and 16-22 have been rejected under 35 U.S.C. §102(b) as anticipated by Greiner *et al.* (1998) *Plant Physiol.* 116:733-742. Specifically, the Examiner has indicated that, given the lack of any limitation on the stringency conditions recited for the antisense molecules disclosed in original claims 2(b), 11(c), 20(c), 21(c), and 22(c), such antisense molecules would include sequences hybridizing under low stringency conditions, including the sequences inherent to the PCR amplification procedures practiced in Greiner *et al.* Applicants have now amended these portions of the claims to recite that the antisense sequences hybridize under high stringency conditions to the nucleotide sequence of SEQ ID NO:1, thereby obviating the rejection, which should be withdrawn.

Page 16 of 25

The Rejection of the Claims Under 35 U.S.C. §103(a), Should Be Withdrawn

Claims 17-18 have been rejected under 35 U.S.C. §103(a) as obvious over Bussis *et al*. (1997) *Planta* 202:126-136 in view of Gordon-Kamm *et al*. (1990) *The Plant Cell* 2:603-618. Specifically, the Examiner has indicated that it would be obvious to combine the teachings of Bussis *et al*. with those of Gordon-Kamm *et al*. to obtain the expression of yeast invertase coding sequences in maize (i.e., monocot) plants and seeds. In light of the amendment to claim 11 to remove any reference to the yeast invertase coding sequence, the rejection has been obviated as it applies to claims 17-18. However, newly presented claims 23-26 similarly recite a yeast invertase gene expressed in a monocot. The rejection as it applies to these claims is respectfully traversed.

At the outset, Applicants note that, as set forth in the *Manual of Patent Examining Procedure* (MPEP) §2141, a showing of obviousness under 35 U.S.C. §103(a) requires that: the claimed invention must be considered as a whole; the references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and, reasonable expectation of success is the standard with which obviousness is determined. With regard to these factors, the Federal Circuit recently reemphasized the importance of the motivation to combine references, stating:

When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. *See*, *e.g.*, *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001) ("the central question is whether there is reason to combine [the] references," a question of fact drawing on the Graham factors).

"The factual inquiry whether to combine references must be thorough and searching." *Id.* It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with. *See*, *e.g.*, *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential component of an obviousness holding") (quoting C.R. Bard, Inc., v. M3 Systems,

Page 17 of 25

Inc., 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998)); In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); In re Dance, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant); In re Fine, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) ("teachings of references can be combined only if there is some suggestion or incentive to do so.") (emphasis in original) (quoting ACS Hosp. Sys., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)).

In re Lee, 61 U.S.P.Q.2d 1430, 1433-4 (Fed. Cir. 2002) (vacating and remanding the decision of the Board for failing to follow the relevant precedent).

In the instant case, the skilled artisan would not be motivated to combine the teachings of Bussis et al. with those of Gordon-Kamm et al., and consequently the rejection of claims 23-26 as obvious should be withdrawn. Specifically, Bussis et al. is directed to a characterization of different lines of potato (dicot) plants expressing the yeast invertase sequence in the apoplast, cytosol, or vacuole cellular compartments, and to a comparison of these results with those obtained by other researchers on another dicot, tobacco. Id. at page 127, first column, last full paragraph. While it is true that the teachings of Bussis et al. could be used in combination with the disclosure of Gordon-Kamm et al. of a method of cereal (monocot) transformation, the focus of Bussis et al. on a comparison of the response of a variety of dicot plant species to the presence of the yeast invertase sequence would hardly suggest to the skilled artisan that a similar study should be undertaken in monocots. Moreover, the simple existence of the method of Gordon-Kamm et al. for transforming a monocot species can hardly be said to provide sufficient motivation to attempt the studies of Bussis et al. in monocots; were this the case, the ability to transform monocots disclosed in Gordon-Kamm et al. would necessarily render obvious every experiment done in any monocot species, a result that clearly cannot be the case. Thus it is clear that there is insufficient motivation to one of ordinary skill in the art to combine the results of

Page 18 of 25

Bussis et al. with those of Gordon-Kamm et al. to obtain the subject matter of new claims 23-26, and the rejection under 35 U.S.C. §103(a) should be withdrawn.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicants respectfully submit that the rejections of the claims under 35 U.S.C. §112, first and second paragraphs, 35 U.S.C. §102, and 35 U.S.C. §103(a) are overcome and should be withdrawn. Applicants submit that this application is now in condition for allowance. Early notice to this effect is solicited. If in the opinion of the Examiner a telephone conference would expedite the prosecution of the application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

Cuchen Asherin

Andrew O. Scheinman Registration No. 50,730

Customer No. 29122 ALSTON & BIRD LLP

Bank of America Plaza 101 South Tryon Street, Suite 4000 Charlotte, NC 28280-4000 Tel Raleigh Office (919) 862-2200 Fax Raleigh Office (919) 862-2260 "Express Mail" Mailing Label Number EL 868643985 US Date of Deposit: **February 24, 2003**

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to:

Commissioner for Patents, Washington, DC 20231.

Muma

Marilyn Muñoz

Page 19 of 25

Version with Markings to Show Changes Made:

Please amend claims 2-7, 11-13, and 20-22 as follows:

- 2. (amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- a) [the]a nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1;
- b) a nucleotide sequence that [corresponds to]is an antisense sequence for the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1, wherein said antisense sequence hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C;
- c) a nucleotide sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1, wherein said nucleotide sequence encodes a polypeptide having invertase inhibitor activity; [and]
- d) a nucleotide sequence that hybridizes to [any one of]the nucleotide sequence [of a) c)]set forth in SEQ ID NO:1 or a complement thereof under [stringent conditions]high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C[, or a complement thereof.]; and
- e) a fragment of at least 50 contiguous nucleotides of the nucleotide sequence set forth in SEQ ID NO:1.
- 3. (amended) The nucleic acid molecule of claim 2, wherein said sequence encodes[an invertase inhibitor having] the amino acid sequence set forth in SEQ ID NO:[2, 5, 8, 11, 14, 17, 20 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, or 53]2.

Page 20 of 25

- 4. (amended) A chimeric gene comprising a <u>plant-functional</u> promoter[capable of driving expression of a sequence in a plant cell] operably linked to [a]the nucleotide sequence of claim 2.
- 5. (amended) The chimeric gene of claim 4, wherein the nucleotide sequence encodes[an invertase inhibitor having] the amino acid sequence set forth in SEQ ID NO:[2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, or 53]2.
- 6. (amended) The chimeric gene of claim 4, wherein said nucleotide sequence is the sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1.
- 7. (amended) The chimeric gene of claim 4, wherein said nucleotide sequence is the antisense sequence of the sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1, wherein said antisense sequence hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C.
- 11. (amended) A transformed plant having incorporated into its genome a DNA molecule, said molecule comprising a nucleotide sequence operably linked to a promoter capable of driving expression of a gene in a plant cell, wherein said nucleotide sequence is selected from the group consisting of:
- a) a sequence encoding an invertase inhibitor having the amino acid sequence set forth in SEQ ID NO: [2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, or 53]2;
- b) the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1;

In re: Helentjaris et al. Appl. No.: 09/780,717 Filed: February 9, 2001 Page 21 of 25

- a nucleotide sequence [that corresponds to]is an antisense sequence for the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1, wherein said antisense sequence hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C;
- d)[a nucleotide sequence that corresponds to an antisense sequence for a plant invertase inhibitor;
- e)] a nucleotide sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54;]1, wherein said nucleotide sequence encodes a polypeptide having invertase inhibitor activity;
 - [f] a nucleotide sequence encoding a yeast invertase enzyme; and
- g)]e) a nucleotide sequence that hybridizes to [any one of]the nucleotide sequence [of a) f)]set forth in SEQ ID NO:1 or a complement thereof under [stringent conditions]high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C[, or a complement thereof.]; and
- f) a fragment of at least 50 contiguous nucleotides of the nucleotide sequence set forth in SEQ ID NO:1.
- 12. (amended) The transformed plant of claim 11, wherein the nucleotide sequence encodes[an invertase inhibitor having] the amino acid sequence set forth in SEQ ID NO:[2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, or 53]2.
- 13. (amended) The transformed plant of claim 11, wherein the nucleotide sequence is the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1.

In re: Helentjaris et al. Appl. No.: 09/780,717 Filed: February 9, 2001 Page 22 of 25

20. (amended) A method for modulating invertase activity in a plant[cell], said method comprising transforming said plant with a DNA construct, said construct comprising a promoter that drives expression in a plant cell operably linked with a nucleotide sequence selected from the group consisting of:

- a) a sequence encoding an invertase inhibitor having the amino acid sequence set forth in SEQ ID NO: [2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, or 53]2;
- b) the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1;
- c) a nucleotide sequence that [corresponds to]is an antisense sequence for the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1, wherein said antisense sequence hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C;
- d)[a nucleotide sequence that corresponds to an antisense sequence for a plant invertase inhibitor;
- e)] a nucleotide sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54;]1, wherein said nucleotide sequence encodes a polypeptide having invertase inhibitor activity;
 - [f] a nucleotide sequence encoding a yeast invertase enzyme; and
- g)]e) a nucleotide sequence that hybridizes to [any one of]the nucleotide sequence [of a) f)]set forth in SEQ ID NO:1 or a complement thereof under [stringent conditions]high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C[, or a complement thereof.]; and

Page 23 of 25

f) a fragment of at least 50 contiguous nucleotides of the nucleotide sequence set forth in SEQ ID NO:1.

- 21. (amended) A method for increasing <u>seed yield</u> in a plant, said method comprising transforming said plant with a DNA construct, said construct comprising a promoter that drives expression in a plant cell operably linked with a nucleotide sequence selected from the group consisting of:
- a) a sequence encoding an invertase inhibitor having the amino acid sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]2;
- b) the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1;
- c) a nucleotide sequence that [corresponds to]is an antisense sequence for the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1, wherein said antisense sequence hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C;
- d)[a nucleotide sequence that corresponds to an antisense sequence for a plant invertase inhibitor;
- e)] a nucleotide sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54;]1, wherein said nucleotide sequence encodes a polypeptide having invertase inhibitor activity;
 - [f] a nucleotide sequence encoding a yeast invertase enzyme; and
- g)]e) a nucleotide sequence that hybridizes to [any one of]the nucleotide sequence [of a) f)]as set forth in SEQ ID NO:1 or a complement thereof under [stringent conditions]high

Page 24 of 25

stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C[, or a complement thereof.]; and

- f) a fragment of at least 50 contiguous nucleotides of the nucleotide sequence set forth in SEQ ID NO:1.
- 22. (amended) A transformed plant cell having incorporated into its genome a DNA molecule, said molecule comprising a promoter capable of driving expression of a gene in a plant cell operably linked to a nucleotide sequence selected from the group consisting of:
- a) a sequence encoding an invertase inhibitor having the amino acid sequence set forth in SEQ ID NO:[2, 5, 8, 11, 14, 17, 20, 23, 26, 29, 32, 35, 38, 41, 44, 47, 50, or 53]2;
- b) the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1;
- c) a nucleotide sequence that [corresponds to]is an antisense sequence for the nucleotide sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54]1, wherein said antisense sequence hybridizes to the nucleotide sequence set forth in SEQ ID NO:1 under high stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C;
- d)[a nucleotide sequence that corresponds to an antisense sequence for a plant invertase inhibitor;
- e)] a nucleotide sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:[1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24, 25, 27, 28, 30, 31, 33, 34, 36, 37, 39, 40, 42, 43, 45, 46, 48, 49, 51, 52, or 54;]1, wherein said nucleotide sequence encodes a polypeptide having invertase inhibitor activity;
 - [f] a nucleotide sequence encoding a yeast invertase enzyme; and
- g)]e) a nucleotide sequence that hybridizes to [any one of]the nucleotide sequence [of a) f)]set forth in SEQ ID NO:1 or a complement thereof under [stringent conditions]high

Page 25 of 25

stringency hybridization conditions of 50% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 0.1X SSC at 60 to 65°C[, or a complement thereof.]; and

f) a fragment of at least 50 contiguous nucleotides of the nucleotide sequence set forth in SEQ ID NO:1.